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IMMUNOLOGY

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inbred strain whose progeny are homozygous at more than 98% of all loci. There are currently over 150 different inbred strains of mice, which are designated by a series of letters and/or numbers (Table 2-1). Most of these strains are purchased by immunologists from such suppliers as Jackson Laboratory in Bar Harbor, Maine. Inbred strains have also been produced in rats, guinea pigs, hamsters, rabbits, and domestic fowl.

Since inbred animals are genetically identical (*syngeneic*), they make it possible to study the immune response in the absence of variables that can be introduced by genetic differences among animals. Once inbred strains became available, immunologists could isolate lymphocyte subpopulations from one animal and inject them into another animal of the same strain. It was with this type of experimental system that immunologists were first able to show that lymphocytes from an antigen-primed animal could transfer immunity to an unprimed syngeneic recipient.

Adoptive-Transfer Systems

In some cases it is important to eliminate the immune responsiveness of the syngeneic host so that the response of only the transferred lymphocytes can be studied in isolation. In adoptive-transfer experiments this is achieved by inactivating the immune cells of the syngeneic recipient. Inactivation can be achieved by exposure to x-rays, to which lymphocytes have been shown to be extremely sensitive. Subjecting a mouse that will serve as host to sublethal doses of x-rays (650–750 rads) can kill 99.99% of its lymphocytes, after which the lymphocytes from the spleen of a syngeneic donor can be studied without interference. In some adoptive-transfer experiments higher x-ray levels are used (900–1000 rads) to eliminate the entire hematopoietic system. This is sometimes necessary if the recipient's hematopoietic cells might influence the adoptive-transfer experiment. The x-irradiated mice will die unless reconstituted with bone marrow from a syngeneic donor.

The adoptive-transfer system has enabled immunologists to study the development of injected lymphoid stem cells in various organs of the recipient. Adoptive-transfer experiments have also facilitated the study of various populations of lymphocytes and of the cellular interactions required to generate an immune response. For example, it was through such experiments that immunologists were first able to show that a T helper cell is necessary for B-cell activation in the humoral response.

Cell-Culture Systems

The complexity of the cellular interactions that generate an immune response has led immunologists to rely heavily on various types of in vitro cell-culture system A variety of cells can be cultured including prima lymphoid cells, cloned lymphoid cell lines, and hybr cells.

Primary Lymphoid Cell Cultures

Primary lymphoid cell cultures can be obtained by is lating lymphocytes directly from blood or lymph or fro various lymphoid organs by tissue dispersion. The ly phocytes can then be grown in a chemically defin basal medium containing saline, sugars, amino acids, tamins, trace elements, and various other nutrients, which various serum supplements are added. Becau in vitro culture techniques require from 10- to 100-fo fewer lymphocytes than typical in vivo techniques, th have enabled immunologists to assess the function properties of minor subpopulations of lymphocytes. was by means of cell-culture techniques, for exampl that immunologists were first able to define the fun tional differences between $CD4^+$ T helper cells ar $CD8^+$ T cytotoxic cells.

Cell-culture techniques have also been used to ide tify various cytokines involved in the activation, growt and differentiation of various cells involved in the in mune response. Early experiments showed that med conditioned by the growth of various lymphocytes antigen-presenting cells would support the growth other lymphoid cells. Many of the individual cytokin that characterized various conditioned media have su sequently been identified and purified, and in many cas the genes encoding them have been cloned. The solub growth factors elaborated by monocytes and macr phages are called *monokines*, and the ones elaborate by lymphocytes are called *lymphokines*. These cyt kines, which play a central role in the activation an regulation of the immune response, are discussed mo fully in Chapter 11.

Cloned Lymphoid Cell Lines

Primary lymphoid cell cultures comprise a heterog neous group of cells which can be propagated only f a limited time. This heterogeneity complicates inte pretation of experiments aimed at understanding th molecular and cellular mechanisms by which lymph cytes generate an immune response. To avoid thes problems immunologists use cloned lymphoid cell lin and hybrid cells.

Normal mammalian cells generally have a finite lif span in culture; that is, after a number of populatio doublings characteristic of the species and cell type, th cells stop dividing. Tumor cells or normal cells tran formed with chemical carcinogens or viruses, howeve